



# UNITED STATES PATENT AND TRADEMARK OFFICE

*dl*  
UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/501,102	02/09/2000	Man Sung Co	WYS-00401	3404

58571 7590 06/25/2007  
FOLEY HOAG, LLP/WYETH  
PATENT GROUP, (w/WYS)  
155 SEAPORT BLVD.  
BOSTON, MA 02210-2600

EXAMINER
----------

GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
----------	--------------

1644

MAIL DATE	DELIVERY MODE
-----------	---------------

06/25/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/501,102	<b>Applicant(s)</b> CO ET AL.	
	<b>Examiner</b> Phillip Gambel	<b>Art Unit</b> 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 143-160 is/are pending in the application.
- 4a) Of the above claim(s) 143, 144, 148 and 155-160 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 145-147 and 149-154 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Art Unit: 1644

### DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action as been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 05/07/2007 has been entered.

Claims 145-147 and 149-154, as they read on the elected invention, including the elected species of the combination of anti-B7-1 antibodies, anti-B7-2 antibodies and cyclosporin or rapamycin in the claimed methods are under consideration in the instant application.

Claims 143-144, 148 and 155-160 have been withdrawn from further consideration by the examiner, 37 C.F.R. 1 § 1.142(b) as being drawn to a nonelected inventions and species.

Claims 1-142 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

This Action will be in response to applicant's request for continued examination under 37 CFR 1.114.

The rejections of record can be found in the previous Office Actions, mailed 04/10/2006, 11/06/2006 and 05/07/2007.

Given the absence of additional rebuttal to the outstanding rejections of record in applicant's request for continued examination under 37 CFR 1.114, the rejections are maintained for the reasons of record.

3. The filing date of the instant claims is deemed as follows.

While It appears that priority USSN 09/249,011, now U.S Patent No. 6,972,125 provides for the recitation of "α CD40 ligands" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see column 18, paragraph 2 of U.S. Patent No. 6,972,125),

this priority document does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient", as broadly claimed in the instant claims.

Art Unit: 1644

While It appears that priority USSN 09/339,596, now U.S Patent No. 6,913,747 provides for the recitation of "anti-CD40 ligands" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see column 24, paragraph 5 of U.S. Patent No. 6,913,747);

this priority document does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient", as broadly claimed in the instant claims.

While It appears that the instant USSN 09/501,102 provides for the recitation of "anti-CD40 pathway inhibitors (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies and small molecule inhibitors of the CD40 pathway" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see page 42, paragraph 2 of the instant specification);

the instant application does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient", as broadly claimed in the instant claims.

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority applications and do change the scope of the instant disclosure as-filed.

Further, neither the priority applications nor the instant application have provides a sufficient description of a representative number of species of "inhibitors of CD40 or CD40 ligand" to represent the entire genus of "inhibitors of CD40 or CD40 ligand", broadly encompassed by the current claims.

For example, it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972). Also see MPEP 2163.05.

Therefore, reliance upon the genus of "drugs" and the disclosure of certain "inhibitors of CD40 or CD40 ligand" (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies) does not provide sufficient written description for certain "inhibitors of CD40 or CD40 ligand", as currently claimed.

Art Unit: 1644

Further, there does not appear to be sufficient description showing possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genera of "α CD40 ligands" "anti-CD40 ligands" and "small molecule inhibitors of the CD40 pathway" consistent with written description provisions of 35 USC 112, first paragraph, and the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday January 2001.

Therefore, there appears to be insufficient written description for the phrase "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient", as broadly claimed in the instant claims in the priority documents as well as in the instant specification.

Therefore, given the lack of written description of the claimed methods as indicated herein and below, the instant claims do not appear to have the priority date of USSNs 09/339,596 and 09/249,011.

If applicant desires priority back to their priority documents, applicant is invited to point out and provide documentary support for the priority of the instant claims.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

A claim as a whole has only one effective filing date.

See Studiengesellschaft Kahle m.b.H. v. Shell Oil Co. 42 USPQ2d 1674, 1677 (Fed. Cir 1997).

4. Claims 145-147 and 149-154 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed:

"wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient".

Applicant's previous amendments simply asserted that no new matter has been added and does not provide any direction to the written support of the newly added claim either in the instant application or in the priority applications.

Art Unit: 1644

The recitation of "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient" is not readily apparent either in the pending or in the earlier priority applications.

While It appears that priority USSN 09/249,011, now U.S Patent No. 6,972,125 provides for the recitation of "α CD40 ligands" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see column 18, paragraph 2 of U.S. Patent No. 6,972,125),

this priority document does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient", as broadly claimed in the instant claims.

While It appears that priority USSN 09/339,596, now U.S Patent No. 6,913,747 provides for the recitation of "anti-CD40 ligands" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see column 24, paragraph 5 of U.S. Patent No. 6,913,747);

this priority document does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient", as broadly claimed in the instant claims.

While It appears that the instant USSN 09/501,102 provides for the recitation of "anti-CD40 pathway inhibitors (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies and small molecule inhibitors of the CD40 pathway" as another drug that can be administered with B7-1- / B7-2-specific antibodies" (e.g., see page 42, paragraph 2 of the instant specification);

the instant application does not provide sufficient written description of the newly amended claim limitation "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient", as broadly claimed in the instant claims.

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority applications and do change the scope of the instant disclosure as-filed.

Further, neither the priority applications nor the instant application have provides a sufficient description of a representative number of species of "inhibitors of CD40 or CD40 ligand" to represent the entire genus of "inhibitors of CD40 or CD40 ligand", broadly encompassed by the current claims.

For example, it cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972). Also see MPEP 2163.05.

Art Unit: 1644

Therefore, reliance upon the genus of "drugs" and the disclosure of certain "inhibitors of CD40 or CD40 ligand" (e.g. anti-CD40 antibodies, anti-CD40 ligand antibodies) does not provide sufficient written description for certain "inhibitors of CD40 or CD40 ligand", as currently claimed.

Further, there does not appear to be sufficient description showing possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genera of "α CD40 ligands" "anti-CD40 ligands" and "small molecule inhibitors of the CD40 pathway" consistent with written description provisions of 35 USC 112, first paragraph, and the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday January 2001.

Given the lack of sufficient description showing possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genera of "α CD40 ligands" "anti-CD40 ligands" and "small molecule inhibitors of the CD40 pathway",

applicant's newly added limitation of reciting a negative limitation based upon the limited disclosure in the instant and priority applications raised new matter under 35 USC 112, first paragraph, written description.

Therefore, there appears to be insufficient written description for the phrase "wherein an inhibitor of CD40 or CD40 ligand is not administered to the transplant recipient", as broadly claimed in the instant claims in the priority documents as well as in the instant specification.

The specification as filed does not provide a sufficient written description or set forth the metes and bounds of this phrase. The specification does not provide blaze marks nor direction for the instant methods encompassing the above-mentioned "limitation", as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above.

See MPEP 714.02 and 2163.06

Art Unit: 1644

Applicant's arguments of record and the examiner's rebuttal are essentially the same of record.

Given the absence of additional rebuttal to the outstanding rejections of record in applicant's request for continued examination under 37 CFR 1.114, the rejections are maintained for the reasons of record.

5. Claims 145-147 and 154 stand rejected under 35 U.S.C § 102(e) as being anticipated by Freeman et al. (U.S. Patent No. 6,605,279) (see entire document).

Freeman et al. teach methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents such as cyclosporine or FK506, including it usefulness in situations of tissue and organ transplantation as well as GVHD (see entire document, particularly Other Therapeutic Reagents on columns 32-34).

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure

Applicant's arguments of record and the examiner's rebuttal are essentially the same of record.

Given the absence of additional rebuttal to the outstanding rejections of record in applicant's request for continued examination under 37 CFR 1.114, the rejections are maintained for the reasons of record.

6. Claims 145-147 and 149-154 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Freeman et al. (U.S. Patent No. 6,605,279) in view of the well known use of immunosuppressives such as cyclosporin, FK506 and rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made, as taught by de Boer et al. (U.S. Patent No. 5,757,034) (1449).

Freeman et al. teach methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents such as cyclosporine or FK506, including it usefulness in situations of tissue and organ transplantation as well as GVHD (see entire document, particularly Other Therapeutic Reagents on columns 32-34).

Art Unit: 1644

While Freeman et al. teach the administration of therapeutically effective amounts of the therapeutic compositions, wherein amounts of effective dosages are administered for periods of time necessary to achieve the desired results (e.g. see Administration of Therapeutic Forms of B Lymphocytes Antigens on columns 37-39), Freeman et al. differs from the claimed methods by not disclosing the well known use of immunosuppressives such as rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made .

De Boer et al. teach the use of B7-specific antibodies in combination with immunosuppressive agents such as cyclosporin, FK506 and rapamycin (e.g., see column 14, paragraphs 2-3) in therapeutic amounts and modes of administration encompassed by the claimed invention (e.g., see column 16, paragraph 5) (see entire document).

One of ordinary skill in the art at the time the invention was made would have been motivated to modify the teachings of Freeman et al. to incorporate the well known use of immunosuppressives such as as cyclosporin, FK506 and rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made to achieve the desired therapeutic result of inhibiting graft rejection and promoting long term graft survival with effective amounts of standard immunosuppressives and effective amounts of therapeutic antibodies. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Also, as to the use of a combination of immunosuppressive therapy in transplantations therapeutic regimens, methods of administration are a result effective variable.

It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

Art Unit: 1644

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 550 U.S. , 2007 U.S. LEXIS 4745, 2007 WL 1237837, at \*12 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Applicant's arguments of record and the examiner's rebuttal are essentially the same of record.

Given the absence of additional rebuttal to the outstanding rejections of record in applicant's request for continued examination under 37 CFR 1.114, the rejections are maintained for the reasons of record.

7. No claim allowed.

8. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Art Unit: 1644

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Phillip Gambel, Ph.D., J.D.  
Primary Examiner  
Technology Center 1600  
June 18, 2007